

REMARKS

Applicants are in receipt of the Examiner's Action dated November 2, 2005, and have the following comments.

Applicants gratefully acknowledge the Examiner's withdrawal of the previous rejection of the claims pursuant to 35 U.S.C. § 103 over Gluchowski (US Patent 5,091,528) and Bishop (US Patent 5,510,398).

Rejection pursuant to 35 USC 103(a)

Claims 21-25 and 27 have now been newly rejected as allegedly *prima facie* obvious over Yavitz (Ocular Surg. News 17:28 supp. 1999) and Woodward (US Patent 5,877,211). Applicants respectfully traverse this rejection for the following reasons.

The present claims are drawn to methods for the use of brimonidine or its derivatives and a prostaglandin for the treatment of the optic nerve and retinal ganglion cells in a mammal suffering from glaucoma or high intraocular pressure. Woodward is characterized as disclosing that certain prostaglandin analogs are neuroprotective, and Yavitz as disclosing that brimonidine prevents optic nerve layer thinning following LASIK laser surgery.

The November 2, 2005 Office Action states that one skilled in the art would have been motivated to combine the teachings of these references "since one relates to the use of [brimonidine]

having neuroprotective activity in the ophthalmic field and the other relates to prostaglandins having neuroprotective activity in the ophthalmic field." Office Action of November 2, 2004 at page 2.

However, neither cited reference suggests combining the two compounds of the present method in a single composition for the protection of retinal ganglion cells or the optic nerve. It is easy to see why this is the case; those of ordinary skill in the art are aware that the combination of glaucoma medications may in certain cases result in adverse side effects limiting their usefulness, and furthermore that any benefit of combination therapy of specific agents is unknown.

For example, as discussed in Searle, Janet B., DRUGS AND AGING 5:156-170(1994) (of record in the present application, and deemed within the knowledge of the person of ordinary skill in the art) "the additivity of prostaglandins to other glaucoma medications is under investigation", even though prostaglandins would "not be expected to be additive" to certain ocular hypotensives.

Similarly, since the prior art such as Searle teaches that the hypotensive activity of certain well-known ocular hypotensives (of which brimonidine is an example) and prostaglandins is "not . . . expected to be additive", there is no reason why other activities (such as neuroprotection) of these agents would be expected to be additive. In light of Searle, there is no motivation provided by the combination of Yavitz or Woodward to combine the agents cited in the present claims in a method for the treatment of the degeneration of retinal ganglion cells or the optic nerve.

An invention is not obvious if the prior art merely contains an invitation to experiment. As made clear by Searle, at most a person of skill in the art considering Yavitz and Woodward might wish to perform the "investigation" (i.e., "experiment") suggested by Searle to see whether these two agents may be used together for a combined neuroprotective effect in subjects suffering from degeneration of the retinal ganglion cells or optic nerve. In light, for example, of the known inflammatory side effects of prostaglandins (see Searle et al.), it was simply unknown whether such one could combine brimonidine and a prostaglandin safely or with any added neuroprotective benefit.

Applicants finally note that they have already overcome this combination of references once; claims 21-27 were free of the prior art (Yavitz and Woodward), cited against the originally filed application, as of the Office Action of November 22, 2004. Applicants respectfully believe that they have demonstrated that the combination of Yavitz and Woodward only tells part of the story; Searle must be considered to be within the purview of the person of ordinary skill in the art, and in light thereof, Yavitz and Woodward provide no more than an invitation to experiment.

Thus, Applicants respectfully maintain that the claims are not obvious over the cited references and respectfully ask that the Examiner again withdraw the pending rejection and permit the claims to proceed to issue.

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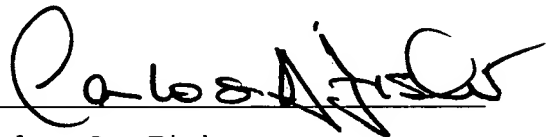
CONCLUSION

For the above reasons, Applicants believe that the present claims are in condition for allowance. Kindly use Deposit Account No. 01-0885 for payment of any fees, including extension fees, required in connection with this reply.

Respectfully submitted,

Dated: 1/4/06

By:

A handwritten signature in black ink, appearing to read 'Carlos A. Fisher', written over a horizontal line.

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